DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (870.1200, formerly §81-2)

Product Manager: 23
MRID No.: 45144401

Reviewer: Byron T. Backus, Ph.D.
Study Completion Date: June 5, 2000
Study No.: MB 00-8314.02

Testing Facility: MB Research Laboratories, Spinnerstown, PA 18968
Author: D.R. Cerven

Quality Assurance (40 CFR §160.12): Included (p. 13)

Test Material: ADMIRAL.WSP; Lot No. 10008; 68.21% blue dye; 4.62% yellow dye
Species: Rabbit; New Zealand White
Age: Young adult (approximately 10-11 weeks old)
Weight: Males: 2.0-2.3 kg; Females: 2.0-2.4 kg
Source: Ace Animals, Inc., Boyertown, PA

Dermal LD_{50} Testing:

Conclusion:

1. **LD_{50} (mg/kg):**
   Males: > 2000 mg/kg (no mortalities at this dose level)
   Females: > 2000 mg/kg (no mortalities at this dose level)
   Combined: > 2000 mg/kg (no mortalities at this dose level)
2. **The estimated LD_{50} is** > 2000 mg/kg
3. **Tox. Category:** III **Classification:** Acceptable

Procedure (including deviations from 870.1200): "The day prior to application of the test article, the dorsal area of the trunk of each animal was clipped free of hair. The prepared site was approximately 10% of the body surface and remained intact... A single dose of the test article was applied to the prepared site at a dose level of 2000 mg active ingredient/kg under a four layered surgical gauze patch measuring 10 x 15 cm and gentle pressure was applied to the gauze to aid in the distribution of the test substance over the prepared site. The torso was wrapped with plastic which was secured with non-irritating tape. The test article remained in contact with the skin for 24 hours at which time the wrappings were removed. Residual test article was removed by gentle washing with distilled water."

Results:

Dosage (mg/kg)[a]	Number of Deaths/Number Tested		
	Males	Females	Combined
2000[b]	0/5	0/5	0/10

[a] At the time of dosing, the test article was weighed and moistened with 3.0 mL distilled water to form a paste.
[b] Dry weight basis

Observations: No rabbits died. "Instances of diarrhea, few feces, soiling of the anogenital area and blue staining of feces were noted during the observation period. Dermal responses were absent to well defined at 24 hours and absent on days 7 and 14. Blue staining of the dose site was noted in all animals. Body weight changes were normal in 9/10 animals. One female lost

weight by day 7 but gained normally by day 14." At 24 hours, one skin site scored 2 for erythema, and two scored 1 for erythema; the same three skin sites also scored positive for edema, with one scoring "2" and two scoring "1." All other skin sites scored zero for both erythema and edema at 24 hours. All skin sites scored zero for both erythema and edema at 7 and 14 days. All dose sites were stained blue from 24 hours through day 14.

Gross Necropsy: "Necropsy revealed treated skin abnormalities in all animals and a kidney abnormality in one male."

Special Comments: The report gives no details as to what the treated skin abnormalities were. Although the study is acceptable in defining a toxicity category III hazard potential in terms of acute dermal toxicity, the Agency should receive more specific information as to what skin abnormalities were observed, as this information might be relevant in any risk assessment for this formulation.

It is also noted that the "blue staining of feces" suggests that appreciable dermal absorption of this formulation can take place.